

Quantification of Mitral Regurgitation by Automated Cardiac Output Measurement: Experimental and Clinical Validation

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Objectives. To develop and validate an automated noninvasive method to quantify mitral regurgitation.

Background. Automated cardiac output measurement (ACM), which integrates digital color Doppler velocities in space and in time, has been validated for the left ventricular (LV) outflow tract but has not been tested for the LV inflow tract or to assess mitral regurgitation (MR).

Methods. First, to validate ACM against a gold standard (ultrasonic flow meter), 8 dogs were studied at 40 different stages of cardiac output (CO). Second, to compare ACM to the LV outflow (ACMa) and inflow (ACMm) tracts, 50 normal volunteers without MR or aortic regurgitation (44 ± 5 years, 31 male) were studied. Third, to compare ACM with the standard pulsed Doppler-two-dimensional echocardiographic (PD-2D) method for quantification of MR, 51 patients (61 ± 14 years, 30 male) with MR were studied.

Results. In the canine studies, CO by ACM (1.32 ± 0.3

liter/min, y) and flow meter (1.35 ± 0.3 liter/min, x) showed good correlation ($r = 0.95$, $y = 0.89x + 0.11$) and agreement ($\Delta CO(y - x) = 0.03 \pm 0.08$ [mean \pm SD] liter/min). In the normal subjects, CO measured by ACMm agreed with CO by ACoMa ($r = 0.90$, $p < 0.0001$, $\Delta CO = -0.09 \pm 0.42$ liter/min), PD ($r = 0.87$, $p < 0.0001$, $\Delta CO = 0.12 \pm 0.49$ liter/min) and 2D ($r = 0.84$, $p < 0.0001$, $\Delta CO = -0.16 \pm 0.48$ liter/min). In the patients, mitral regurgitant volume (MRV) by ACMm-ACMa agreed with PD-2D ($r = 0.88$, $y = 0.88x + 6.6$, $p < 0.0001$, $\Delta MRV = 2.68 \pm 9.7$ ml).

Conclusions. We determined that ACM is a feasible new method for quantifying LV outflow and inflow volume to measure MRV and that ACM automatically performs calculations that are equivalent to more time-consuming Doppler and 2D measurements. Additionally, ACM should improve MR quantification in routine clinical practice.

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The severity of mitral regurgitation (MR) is a major determinant for mortality and the timing of surgical intervention (1). In recent years, patients with MR have been referred for surgical intervention earlier in the course of their disease (2), reflecting improvements in valve repair surgery and the low risk for this procedure (0% mortality in 595 primary, isolated mitral valve repairs over the past 4 years at the Cleveland Clinic Foundation) (3). Accurate estimation of MR volume (MRV) and left ventricular function is critical to optimizing the timing of surgery (4–6). Although quantitative left ventriculography has historically been considered the reference standard for regurgitant volume, in practice it is rarely performed and certainly is not feasible for sequential measurements. A variety of noninvasive techniques have been developed using Doppler echocardiography (7–15), but the

quantification of mitral valvular regurgitation remains problematic and is rarely performed clinically.

A new technique has recently been developed for automated cardiac output measurement (ACM), using digital velocities from a color Doppler flow map, integrated in space and time across the left ventricular outflow tract throughout systole (16). We have validated this method against several measures of cardiac output (CO) in a large group of patients and normal subjects (17), but to date this approach has not been extended to the left ventricular inflow tract, which potentially could facilitate quantification of MR. The purpose of this study, therefore, was 1) to validate more rigorously than our previous study the fundamental accuracy of ACM in an animal model, 2) to demonstrate the equivalency of cardiac stroke volume (SV) measurements across the left ventricular inflow and outflow tracts in a group of normal volunteers and 3) to validate the accuracy of this new method to quantify MRV as the difference in mitral and aortic SVs in a group of patients.

Methods

Animal study. Cardiac output was measured using both echocardiographic (ACM) and aortic flow probe techniques in

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Abbreviations and Acronyms

ACM	= automated stroke volume or cardiac output measurement
ACMa	= automated stroke volume or cardiac output measurement through the left ventricular outflow tract
ACMm	= automated stroke volume or cardiac output measurement through the mitral annulus
CO	= cardiac output
MR	= mitral regurgitation
MRV	= mitral regurgitation volume
PD	= pulsed Doppler measurement of stroke volume or cardiac output through the aortic annulus
SV	= stroke volume
2D	= left ventricular stroke volume or cardiac output calculated by two-dimensional echocardiography

a series of experiments using 8 adult mongrel dogs (38 ± 8 kg) at 40 different stages of CO. The dogs were anesthetized with intravenous sodium pentobarbital (25 mg/kg), intubated and ventilated using room air. A peripheral vein and the right femoral artery were cannulated for administration of medication and hemodynamic monitoring. Arterial pressure was measured using fluid-filled catheters and monitored throughout the experiments. After a midline sternotomy, the sternum was split widely and the heart suspended in a pericardial cradle, ensuring an adequate echocardiographic imaging window. An aortic flow probe (AP20A) (Transonic Systems Inc., Ithaca, New York) was positioned around the ascending aorta and connected to the Transonic HT207 Flowmeter for continuous CO measurement. A PSK-37 AT 3.75 MHz transducer was used with a Toshiba SSA-380A (Nasu, Japan) equipped with ACM functionality.

We performed ACM in the left ventricular outflow tract from an apical long-axis view, with color baseline shifting to avoid aliasing. Cardiac output was varied in each dog with variations in intravascular volume and afterload (using intravenous nitroprusside and phenylephrine infusions).

Two-dimensional (2D) color Doppler flow imaging of left ventricular outflow over several cardiac cycles was acquired into memory, and ACM volumetric flow rate was calculated by double integration of Doppler signals in space (across the left ventricular outflow tract) and in time (through the systolic period). Reference CO was obtained simultaneously by the ultrasonic flow probe around the ascending aorta.

Study population. The clinical study was conducted on two populations: 1) normal volunteers, determined by echocardiography to be without valvular dysfunction ($n = 50$, 44 ± 5 years, 31 male) and 2) patients with at least mild MR by 2D Doppler color flow imaging and without valvular prosthesis, mitral stenosis or aortic stenosis or regurgitation ($n = 51$, 61 ± 14 years, 30 male). Diagnoses for these patients included mitral valve prolapse ($n = 30$, bileaflets in 17, anterior in 5 and posterior in 8 [2 flails]), coronary artery disease ($n = 17$), cardiomyopathy ($n = 2$), rheumatic valvular disease ($n = 1$)

and endocarditis with ruptured chordae ($n = 1$). Twenty patients had an eccentric jet, 13 of which were anteriorly directed, and the remaining 31 had a central jet.

Echocardiography. All volunteers and patients underwent a complete 2D echocardiographic and Doppler study in the left lateral decubitus position from multiple windows. Studies were performed with a Toshiba SSA-380A echocardiograph equipped for ACM and were recorded on 0.5-in VHS tape. The SV was measured by four methods as detailed below, then multiplied by the heart rate to obtain CO: 1) ACM by spatiotemporal color Doppler flow integration across the left ventricular outflow tract from the apical long axis view (ACMa), 2) the left ventricular inflow tract from apical four- and two-chamber views (ACMm), 3) the difference in volume of manually traced end-diastolic and end-systolic 2D echocardiographic images and 4) pulsed Doppler (PD) measured flow at the aortic valve level. The MR volume was obtained in two ways: 1) ACMm – ACPa and 2) 2D-PD. A qualitative grade of MR severity was obtained from the clinical echocardiography report, which was based on a visual impression combining the variables of jet area, jet direction, proximal jet width, left atrial size, pulmonary venous flow and mitral valve morphology.

Automated cardiac output measurement. To avoid aliasing, the color baseline was shifted until all flow in the left ventricular outflow tract during systole was coded blue (for ACPa) or was uniformly red within the left ventricular inflow tract during diastole (for ACMm). Images were obtained from apical long axis view (for ACPa), and the apical four- and two-chamber views (for ACMm) using a 2.5 MHz probe. The systolic and diastolic periods were defined by manual triggers based on the electrocardiogram and color flow. A region of interest was placed across the left ventricular outflow tract at the mitral annulus level during systole (for ACPa) and across the left ventricular inflow tract at the mitral annulus during diastole (for ACMm) (Fig. 1). Frame rate typically was 28 to 35 Hz. Volumetric flow rate was calculated by double integration of Doppler data in space (across the left ventricular outflow or inflow tract) and in time (through systole or diastole), assuming hemiaxial symmetry: $\int \int \pi r v(r,t) dr dt$, where $v(r,t)$ is the velocity at a distance r from the center of the left ventricular outflow tract and at time t during systole or the center of the left ventricular inflow tract at time t during diastole. For diastolic inflow, the SVs were measured from the apical four- and two-chamber views and averaged. This technique was performed by an investigator blinded to the results of other methods.

Doppler and two-dimensional echocardiographic techniques. Aortic SV was measured by PD echocardiography performed with the sample volume positioned at the aortic valve annulus from the apical long axis view. The aortic annular diameter D was measured in the parasternal long axis view from the anterior to the posterior hinge point of the aortic valve, and the cross-sectional area derived as $\pi D^2/4$. The time-velocity integral of aortic flow was measured by manually tracing the PD recording on line and multiplied by annular

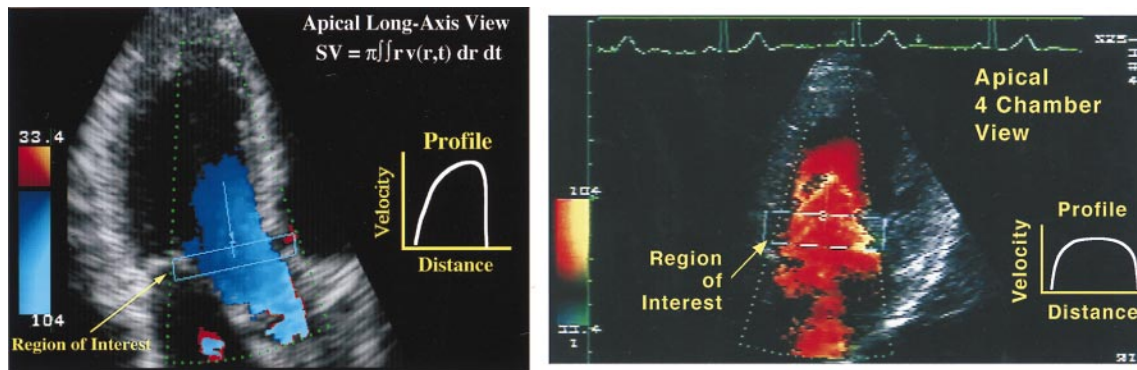


Figure 1. Blood flow through left ventricular outflow (left) and inflow (right) tracts. Forward SV is calculated by integrating velocity in space and time throughout systole and diastole, respectively.

area to yield SV. Left ventricular SV was also calculated as the difference in systolic and diastolic ventricular volume, assessed from the apical four-chamber view using Simpson's rule approximation (2D). For the normal volunteers, the difference between aortic and left ventricular SV should have been zero, while for the MR patients it provided a reference standard against which to compare the ACM calculations.

Color Doppler mapping was performed from the parasternal long-axis, apical four- and two-chamber views. For jet areas, an optimal gain setting was obtained by maximizing the gain level without introducing signals in the nonflow areas. Images were scanned frame by frame to find the largest regurgitant jet area (18,19). The traced jet area included the centrally aliased and peripherally nonaliased signals. When it was possible, left atrial area was traced in the same frame in which the maximal jet area was seen.

Vena contracta width was measured in 26 patients with MR, as previously described (7). In this group, for each echocardiographic window, zoom mode was used to optimize visualization and measurement of the vena contracta. To account for the possibility of asymmetric orifices, vena contracta width was measured from apical two- and four-chamber views.

In addition to ventricular systolic and diastolic volume, maximal left atrial area was measured from the apical four-chamber view. Left atrial and ventricular diameters were measured by M-mode or 2D imaging from the parasternal long axis view. All echocardiographic data were measured on line, with the PD and 2D assessments performed by an investigator blinded to the ACM results.

Observer agreement. In 20 randomly selected volunteers and patients (without MR), two observers independently measured the CO using ACMA and ACMm, and interobserver agreement was assessed by linear regression and analysis of agreement (20). These same studies were also reexamined by

one observer at a separate time to determine intraobserver agreement. Interobserver and intraobserver variability were also assessed for the difference in ACMm and ACMA (the MRV, which should be zero in this population).

Impact of gain. We have previously demonstrated the impact of gain on ACM data in the left ventricular outflow tract (17). To address this issue for the inflow tract, 10 subjects (4 male, 39 ± 9 years) underwent ACM examination of transmitral flow underwent three conditions: 1) reduced gain (color dropout seen in the inflow tract); 2) visually optimal gain (uniform color seen throughout the inflow tract but not outside it); and 3) excessive gain ("blooming" of color and thermal noise seen outside the inflow tract).

Statistical analysis. All values were averaged from three to five beats and expressed as mean \pm SD. Least-squares linear regression analysis and analysis of agreement (20) were used to compare 1) CO by ACM with flow meter in the animal studies, 2) ACMA with ACMm CO in the normal volunteers and 3) MRV derived by ACMm-ACMA SV with the difference of 2D and PD SV.

Analysis of variance (ANOVA) and Spearman rank correlation were used to compare the qualitative echocardiographic grading of MR with MRV, regurgitant fraction (MRV/ACMm), left atrial diameter, left atrial area, left ventricular dimension, maximal jet area, vena contracta width and the ratio of pulmonary S and D waves. When ANOVA was significant, mean group differences were compared using Bonferroni contrast. Simple and multiple linear regression were used to investigate the correlation between MRV and other estimates of regurgitant severity.

Repeated measures ANOVA was used to characterize the impact of gain in the 10 subjects studied.

Results

Animal study. For 40 stages in 8 dogs, CO averaged 1.32 ± 0.3 liter/min by ACM and 1.35 ± 0.3 liter/min by flow meter. Good correlation and agreement were seen between ACM (y) and flow meter (x) measurements of CO: $r = 0.95$, $y = 0.89x + 0.11$, $\Delta\text{CO} = -0.03 \pm 0.08$ liter/min (Fig. 2).

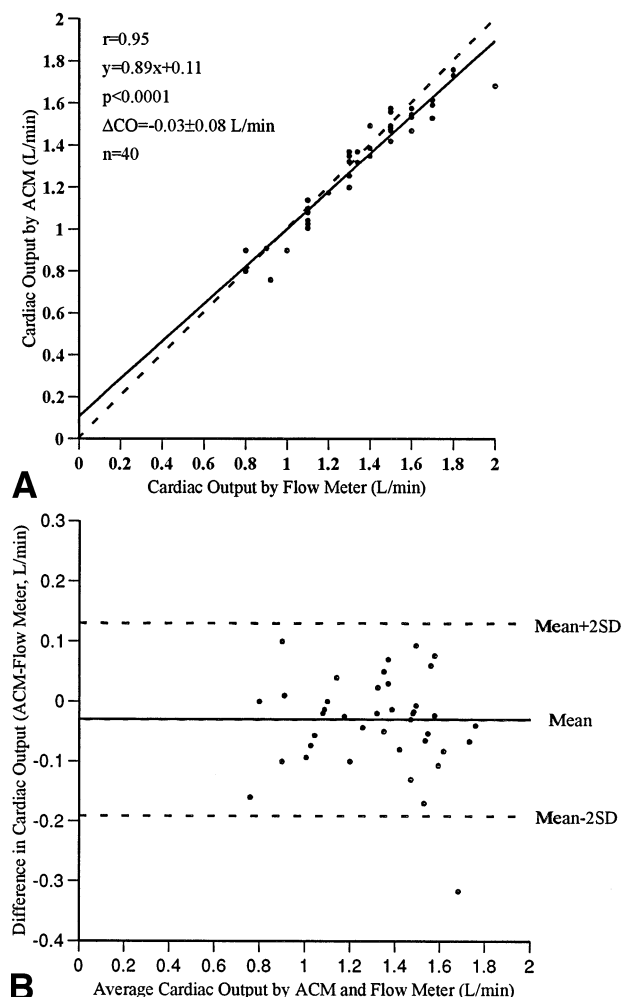


Figure 2. Regression (top) and agreement (bottom) plots comparing CO by ACM and flow meter in animal study.

Human studies. Feasibility. Cardiac output was successfully determined by using ACM in 51 of 53 patients (96%) it was attempted in, and feasible in all 50 volunteers. Pulmonary venous flow was successfully measured in all 51 MR patients. Vena contracta measurement was performed in 26 patients. Table 1 summarizes the echocardiographic variables measured in this study.

Volunteer group. As shown in Fig. 3, in the normal subjects, CO measured by ACMm was closely approximated by ACMA ($r = 0.90$, $p < 0.0001$, ΔCO [ACMm – ACMA] = -0.09 ± 0.42 liter/min), by PD ($r = 0.87$, $p < 0.0001$, ΔCO [ACMm – PD] = -0.16 ± 0.48 liter/min) and by 2D ($r = 0.84$, $p < 0.0001$, ΔCO [ACMm – 2D] = -0.12 ± 0.49 liter/min).

Patients. Based on the qualitative grading of MR, 8 patients had mild MR, 19 patients had moderate MR and 24 had severe MR. As shown in Fig. 4, MRV (ACMm – ACMA) was well correlated with 2D-PD ($r = 0.88$, $y =$

Table 1. Echocardiographic Variables in Patients With Mitral Regurgitation

Variable	Mean \pm SD	Range
LAD (cm)	4.4 ± 0.8	2.6–6.4
LAA (cm ²)	27.1 ± 7.5	12.0–50.0
LVEDD (cm)	5.8 ± 0.7	4.9–8
EDV (ml)	148.2 ± 47.6	73–260
ESV (ml)	61.5 ± 40.6	11–181
MRV, ACM (ml)	35.3 ± 19.8	3.3–86
RF, ACM	0.37 ± 0.14	0.07–0.64
MRV, 2D-PD (ml)	32.6 ± 19.8	3.3–86
RF, 2D-PD	0.36 ± 0.15	0.02–0.68
Maximal jet area (cm ²)	10.5 ± 5.6	1.8–28
VCW PLAX (cm)	0.47 ± 0.19	0.15–0.86
VCW 4-chamber (cm)	0.44 ± 0.13	0.27–0.78
Average VCW (cm)	0.46 ± 0.13	0.21–0.69
Pulmonary vein SPV (m/s)	0.42 ± 0.22	0.11–0.91
Pulmonary vein DPV (m/s)	0.53 ± 0.27	0.2–0.93
Pulmonary vein S/D (PV)	0.87 ± 0.42	0.17–1.98

DPV = D wave peak velocity; EDV = left ventricular end-diastolic volume; ESV = left ventricular end-systolic volume; LAA = left atrial area; LAD = left atrial diameter; LVEDD = left ventricular end-diastolic diameter; MRV = mitral regurgitant volume; PLAX = parasternal long-axis; RF = regurgitant fraction; SPV = S wave peak velocity; VCW = vena contracta width.

$0.88x + 6.6$, $p < 0.0001$), with good agreement seen ($\Delta MRV = ACM - (2D-PD) = 2.68 \pm 9.7$ ml).

Correlations between MRV and other regurgitant parameters are shown in Table 2. No single parameter had an r^2 exceeding 0.4 for predicting MRV, and the traditional indices of jet area, vena contracta width and pulmonary venous S/D ratio were particularly poor. Even combining five parameters (left ventricular and left atrial diameter, jet area, vena contracta width and pulmonary venous S/D ratio) in a multivariate model yielded an r^2 of only 0.55. Interestingly, the clinical grading of regurgitant severity, which integrates all of these parameters, showed superior correlation with MRV with $\rho = 0.78$ (Table 3, Fig. 5). The values of various parameters for each qualitative grade of MR are shown in Table 3.

Reproducibility of results. The relative and absolute interobserver variability for CO by ACM were $1.5\% \pm 4.6\%$ (absolute range, 0.4% to 11.6%) and 0.09 ± 0.23 liter/min (range, 0.02 to 0.61 liter/min), respectively, with good correlation ($r = 0.94$, $y = 0.9x + 0.15$, $p < 0.0001$) liter/min). Intraobserver measurements similarly showed acceptable variability ($2.2\% \pm 4.2\%$ and 0.1 ± 0.2 liter/min; ranges 0.1% to 6.8% and 0.09 to 0.34 liter/min) and correlation ($r = 0.96$, $y = 0.94x + 0.39$, $p < 0.0001$). Table 4 summarizes the intraobserver and interobserver variation for mitral and aortic SV by ACM. Also shown is the reproducibility for the “regurgitant” volume, which should average zero in these subjects without MR. Note that there is a positive (though weak) correlation, indicating some tendency for patients to have similar degrees

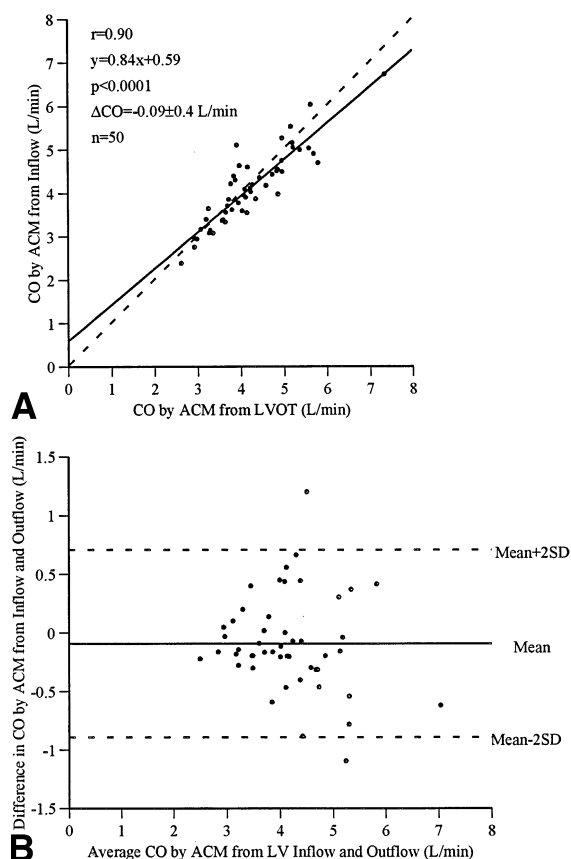


Figure 3. Regression (top) and difference (bottom) plots comparing CO by ACM from inflow vs. outflow in normal volunteers without regurgitation.

of overestimation or underestimation on successive examinations.

Impact of gain. When gain was optimized so color was seen throughout the inflow tract and nowhere else (typically at a setting of 16 to 17 on the 0 to 30 scale of the instrument), SV was 52 ± 13 ml. With gain reduced to cause color dropout, SV was 17 ± 9 ml less, while it was 16 ± 11 ml more when excessive gain caused color to be seen outside the lumen ($p = 0.02$ by repeated measures ANOVA).

Discussion

Mitral regurgitation is a common problem in clinical practice. Because accurate assessment of regurgitant magnitude is critically important to clinical management, including the

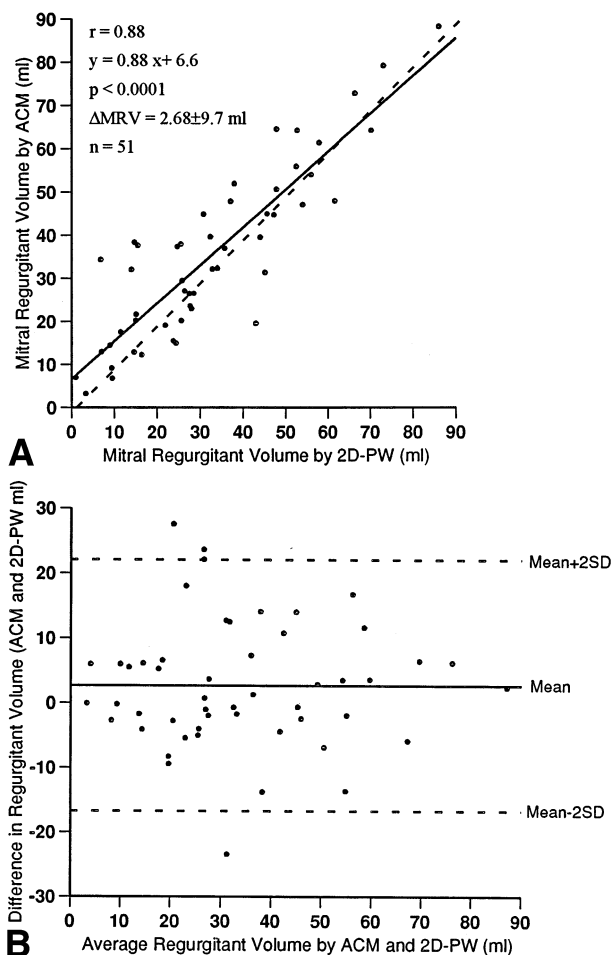


Figure 4. Regression (top) and difference (bottom) plots comparing MRV measured by ACM with 2D-PD method in clinical patients.

timing of surgical intervention, many quantitative methods have been proposed, using echocardiographic, angiographic, nuclear and magnetic resonance data. These techniques unfortunately are applied inconsistently in routine clinical practice.

Echocardiographic techniques for quantitating MR include momentum analysis (using either color Doppler data [21] or the centerline jet velocity decay [22]), proximal convergence analysis (15,23), use of amplitude-weighted mean velocities from continuous-wave Doppler spectra (24), and PD measurement of SV through the mitral annulus and left ventricular outflow tract (25). Comparison of mitral and left ventricular outflow tract SV, which rely on the continuity equation, is the most established of these techniques, but this approach re-

Table 2. Correlation Coefficient Between Mitral Regurgitant Volume (by ACM) and Related Factors

Variable	LVD	LVA	LAD	LAA	VCW	Jet Area	PV S/D
r	0.63	0.47	0.53	0.53	0.43	0.39	0.28
p	< 0.0001	0.0012	< 0.0001	< 0.0001	0.027	0.058	0.087

LVA = left ventricular area; LVD = left ventricular diameter; PV S/D = pulmonary venous S/D ratio. See Table 1 for remaining abbreviations.

Table 3. Correlation Coefficient Between Qualitative Grading of Mitral Regurgitant Severity and Related Factors

Variable	ANOVA					Spearman Rank Correlation	
	Mild	Moderate	Severe	F	P	ρ	p
RV, ACM (ml)	9.9 ± 3.9	29.2 ± 12.4	48.6 ± 16.9	25.6	< 0.0001	0.78	< 0.0001
RF, ACM	0.17 ± 0.1	0.35 ± 0.11	0.46 ± 0.09	30.3	< 0.0001	0.72	< 0.0001
LAA (cm ²)	17.0 ± 2.9	25.2 ± 4.4	31.5 ± 6.3	23.9	< 0.0001	0.76	< 0.0001
LAD (cm)	3.2 ± 5.1	4.1 ± 5.6	4.9 ± 6.3	24.3	< 0.0001	0.73	< 0.0001
Jet area (cm ²)	4.2 ± 2.2	9.1 ± 3.2	13.6 ± 5.6	14.9	< 0.0001	0.67	< 0.0001
LVEDD (cm)	42.4 ± 8.0	49.8 ± 5.9	57.8 ± 6.5	17.4	< 0.0001	0.57	< 0.0001
VCW (mm)	3.4 ± 0.2	4.1 ± 0.7	4.8 ± 1.1	1.9	=0.17	0.47	=0.18
PV S/D (cm)	1.1 ± 0.5	0.98 ± 0.44	0.74 ± 0.34	2.4	=0.1	0.19	=0.2

ACM = automated cardiac output measurements; RV = regurgitant volume. See Tables 1 and 2 for remaining abbreviations.

quires meticulous care, particularly in positioning the Doppler sample volumes. Studies of proximal convergence analysis have reported good results (9,13–15,23,26,27), but this method has limitations, mostly related to the geometry of the flow convergence region. Close to the orifice, isovelocity contours flatten out, and the hemispheric formula will predictably underestimate the true flow rate (28). Conversely, nearby walls can push isovelocity contours outward and cause flow overestimation (14,15). With these limitations, the need for new practical methods to quantify MRV is evident, prompting the current study.

In a previous study (17), automated integration of color Doppler velocity was shown to be an accurate noninvasive method for measuring CO in a large group of normal volunteers and intensive care unit patients. The accuracy of this method in the left ventricular outflow tract prompted the current study, where we attempted to use the automated method for flow across the mitral annulus in hopes of quantifying MRV. This technique was feasible in all 50 volunteers for determining SV from both the left ventricular outflow and inflow tracts, with excellent correlation and agreement, suggesting that MRV could be accurately determined as inflow minus outflow SV. The results demonstrated that this approach agrees well with more cumbersome conventional methods for quantifying MRV.

Comparison with other methods. *Two-dimensional echocardiography combined with Doppler-echocardiography.* Two-dimensional echocardiography estimates of ventricular volume can be combined with Doppler-echocardiographic determinations of aortic flow to calculate regurgitant volume and fraction in patients with MR (27). The forward SV is obtained as the product of aortic velocity time integral and aortic annular area, shown to be accurate ($r = 0.84$ to 0.97) in a variety of studies (29–32). Comparable agreement was obtained in the current and previous (17) studies of ACM, with the advantage of obtaining the measurement from a single echocardiographic window.

Left ventricular SV can be calculated by measuring end-

diastolic and end-systolic volumes from 2D echocardiography. Such an approach requires an assumption of left ventricular geometry and is often limited by poor endocardial definition. Automated boundary detection has been used to quantify left ventricular volumes, ejection fraction and CO, and have shown to be feasible and accurate in most patients (33,34) but subject to the same geometric assumptions and image quality requirements as the standard 2D methods.

Given 2D and PD estimates of SV, MRV is given by 2D-PD with regurgitant fraction calculated as $(SV_{2D} - SV_{Ao})/SV_{2D}$. Compared with prior studies, comparable agreement was observed for the inflow-outflow ACM method in calculating regurgitant volume but was significantly less time-consuming than the 2D-PD method. Interestingly, the cases with the greatest discrepancy between ACM and 2D-PD estimates of regurgitant volume were consistently seen in the most significantly dilated ventricles. In general, the qualitative MR grading in these cases agreed more closely with ACM, suggesting that SV in these ventricles was erroneously estimated by 2D, due perhaps to the enlarged and altered geometry.

Mitral regurgitant jet area. Because of its simplicity and ease of use, simple visual assessment of the color Doppler-defined regurgitant jet is the most common method in practice. The mitral regurgitant jet area has been shown to correlate with angiographic grading of MR (35–38). In our study, the jet area was correlated reasonably well with the qualitative grading of MR ($F = 14.9$, $p = 0.0001$; $\rho = 0.67$, $p < 0.0001$), but showed poor correlation (0.39) with quantitative MRV.

Building on the work of Mele et al. (39), Hall et al. (7) reported that careful color flow mapping of the vena contracta of the mitral regurgitant jet provides a simple estimate of the regurgitant orifice area that correlates reasonably well with quantitative Doppler techniques. However, because the regurgitant mitral orifice is often irregularly shaped, multiplying two biplane diameters to calculate the regurgitant orifice area may overestimate or underestimate the actual area (7). In the current study, the vena contracta was only modestly correlated with the regurgitant volume ($r = 0.43$).

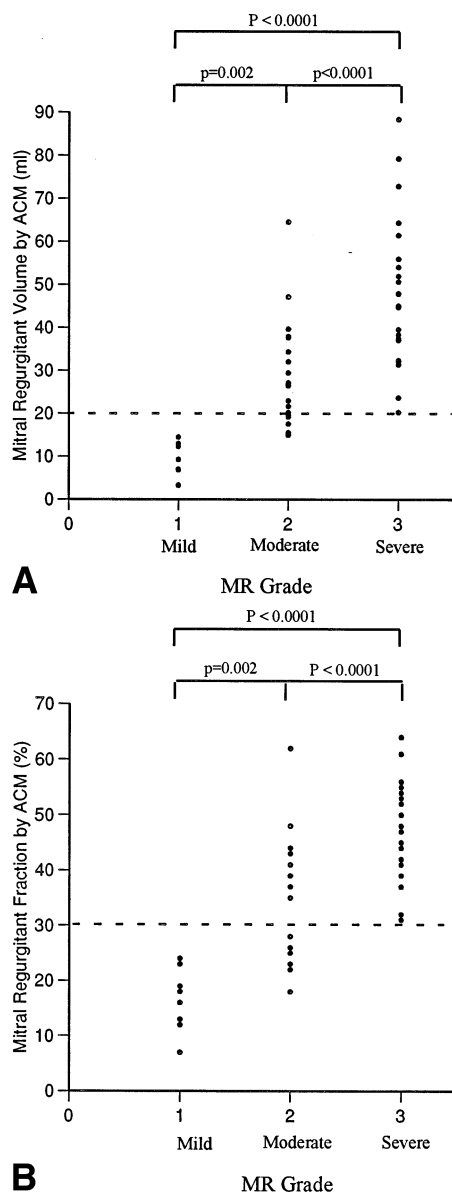


Figure 5. Values of regurgitant volume (**top**) and regurgitant fraction (**bottom**) (y axis) were compared with the qualitative grading of mitral regurgitant (MR) severity (x axis). Although the mean values were statistically significantly different among grades, considerable overlap is present.

Pulmonary venous flow patterns have previously been used to assess MR severity, but showed relatively poor correlation in the current study. This likely reflects the difficulties in quanti-

tative pulmonary venous measurements from the transthoracic window in comparison to the transesophageal approach used in prior studies (12,40).

Interestingly, the best correlation ($\rho = 0.78$) was seen between MRV and the clinical grading of regurgitant severity. Apparently, this “eyeball” approach, which integrates jet area and eccentricity, chamber size and pulmonary venous flow pattern, performs considerably better than did any of those parameters by themselves, though certainly not as good as a truly quantitative assessment.

It should be noted that the proximal convergence method was not directly compared to ACM in this study, primarily due to logistical reasons and a desire to maintain compatibility with prior ACM validation (17) that used 2D and PD methods as the principal reference methods. In general, proximal convergence is an excellent approach to quantify MR, especially when regurgitant volume is relatively small where 2D and PD methods that rely on subtracting large numbers from each other may yield proportionally larger errors.

Limitation of the study. Like all clinical studies of MR, this one had no true gold standard against which to test the new method. The 2D-PD method is not optimal, assuming as it does symmetric ventricular geometry and a flat velocity profile in the left ventricular outflow tract. Automated cardiac output measurement avoids the assumption of a flat profile, but does assume hemiaxial symmetry that likely is not strictly true, especially in markedly distorted left ventricular outflow tract geometry such as hypertrophic cardiomyopathy; no such patients were included in this study. Automated cardiac output measurement further requires unaliased velocity and extraneous flow outside the vessel included in the region of interest. For example, an anteriorly directed MR jet might flow adjacent to the left ventricular outflow tract and thus be included in the outflow estimation, or aortic insufficiency might contaminate the inflow calculations. Our prior study (17) demonstrated an unsurprising gain dependence of the method for left ventricular outflow tract measurements. In the current study we extended this observation to the inflow tract, confirming that ACM can generally be optimized simply by adjusting gain until the color fills the region of interest but is not seen in the adjacent walls (typically at gain settings of 16 or 17 on a 0 to 30 scale). Automated cardiac output measurement is relatively tolerant of Doppler misalignment with flow: we previously showed $<5\%$ error for misalignment up to 30° (17).

We specifically excluded patients with only trivial MR, studying only those at least mild in magnitude, shown previ-

Table 4. Interobserver and Intraobserver Variability

	Interobserver			Intraobserver		
	SVa	SVm	RV	SVa	SVm	RV
r	0.95	0.89	0.63	0.93	0.94	0.60
Δ SV (ml)	0.3 ± 3.1	0.1 ± 3.7	0.47 ± 5.32	1.3 ± 3.1	0.3 ± 3.9	1.54 ± 3.76

Data are mean \pm SD. RV = regurgitant volume; SVa = aortic stroke volume; SVm = mitral stroke volume.

ously to have a regurgitant volume of 25 ± 13 ml (41). This may explain why none of the regurgitant volume calculations (by ACM or 2D-PD) were negative, despite known scatter in each measurement from the normal volunteers.

Clinical implications and future directions. Clearly, if a method such as this can measure MR, one should be able to reverse the order of subtraction and quantify aortic regurgitation (though not mixed disease, since neither the inflow nor outflow SV would be suitable as a reference for net forward flow). Similarly, application of this method to the left ventricular outflow tract and right ventricular outflow tract should allow characterization of intracardiac shunts. The ease with which ACM can be integrated into a clinical examination should encourage its routine use in echocardiography.

Conclusions. Automatic integration of numerical data within color Doppler flow fields is feasible for measuring SV in the left ventricular inflow and outflow tracts. We have further shown that the difference of these SVs may be used to estimate MRV, which appears to be simpler and faster than other noninvasive techniques.

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